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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/521,576   | 06/29/2005  | Toshitada Noguchi    | 2005_0034A          | 4025             |
| 513 7590 03/31/2008<br>WENDEROTH, LIND & PONACK, L.L.P.<br>2033 K STREET N. W.<br>SUITE 800<br>WASHINGTON, DC 20006-1021 |             |                      |                     |                  |
| EXAMINER   |             |                      |                     |                  |
| ARIANI, KADE   |             |                      |                     |                  |
| ART UNIT   |             | PAPER NUMBER         |                     |                  |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/521,576

**Applicant(s)**

NOGUCHI ET AL.

**Examiner**

KADE ARIANI

**Art Unit**

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SF 298)  
Paper No(s)/Mail Date 1/18/2005
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_

### ***DETAILED ACTION***

The preliminary amendment filed on June 29, 2005, has been received and entered.

Claims 1-7 are pending in this application and were examined on their merits.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-4 and 6-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitations "...cells or processed products thereof are employed as the ...epimerase, NeuAc synthase...." in claims 3 and 6, are confusing, it is unclear which is it that the applicant is trying to claim in the method, a transformant, a processed product of cells, or the enzymes therefore claims 3 and 6 are indefinite.

The recitations "... and a processed product of cells ...as the CMP-NeuAc synthase" in claims 4 and 7 are confusing, it is unclear which is it that the applicant is trying to claim in the method, a transformant, a processed product of cells, or the enzymes therefore claims 6-7 are indefinite.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koizumi et al. (US 2002/0064836 A1) in view of Plumbridge & Vimr (Journal of Bacteriology, 1999, Vol. 181, No.1. p47-54), and further in view of Ishige et al. (in IDS, Biosci. Biotechnol. Biochem., 2001, Vol. 65, No. 8, p.1736-1740), and Tabata et al. (Enzyme & Microbial Technology, March 2002, Vol. 30, p.237-333).

Claims 1-4 are drawn to a process for producing CMP-N-acetylneuraminic acid (CMP-NeuAc), comprises adding yeast cells, N-acetylglucosamine-6-phosphate 2-epimerase (GlcNAc-6P-2-epimerase), N-acetylneuraminic acid lyase (NeuAc lyase), and CMP-N-acetylneuraminic acid synthase (CMP-NeuAc synthase) to a reaction system containing N-acetylglucosamine (GlcNAc), pyruvate, and cytidine 5'-monophosphate (CMP), and inducing reaction of the mixture.

Claims 5-7 are drawn to a process for producing CMP-N-acetylneuraminic acid (CMP-NeuAc), comprises adding yeast cells, N-acetylglucosamine-6-phosphate 2-epimerase (GlcNAc-6P-2-epimerase), N-acetylneuraminic acid synthase (NeuAc synthase), and CMP-N-acetylneuraminic acid synthase (CMP-NeuAc synthase) to a reaction system containing N-acetylglucosamine (GlcNAc) and cytidine 5'-monophosphate (CMP), and inducing reaction of the mixture.

Koizumi et al. teach a process for producing CMP-N-acetylneuraminic acid (CMP-NeuAc), comprises adding yeast cell (page 7 0103), N-acetylneuraminic acid aldolase (also called NeuAc lyase), and CMP-N-acetylneuraminic acid synthase (CMP-NeuAc synthase), N-acetylneuraminic acid synthase (NeuAc synthase) (page 2 0026, Table 1.) to a reaction system containing N-acetylglucosamine (GlcNAc), pyruvate, and cytidine 5'-monophosphate (CMP) (page 8-9 0126, 0127, and 0128), and inducing reaction of the mixture.

Koizumi et al. also teach the process is useful for the production of complex carbohydrates which is useful for protection against infection of bacteria, viruses, and the like, application to cardiovascular disorders and immunotherapy, and a process which uses inexpensive nucleotide precursors, sugars, and complex carbohydrate precursors as the starting material (page 1 0001 and 0005, page 13 0185-0197).

Koizumi et al. do not teach adding N-acetylglucosamine-6-phosphate 2-epimerase (GlcNAc-6P-2-epimerase) in the reaction mixture. However, Plumbridge & Vimr teach GlcNAc-6P-2-epimerase involvement in the metabolism of N-acetylneuraminic acid (sialic acid) and catalyzed the conversion of N-acetylmannosamine 6-phosphate to N-acetylglucosamine 6-phosphate (see Abstract and p.48 Fig.1.).

Plumbridge & Vimr further teach the existence of the putative gene for the ManNAc kinase and epimerase function within the *nanAT* operon allows the metabolic pathway for use of sialic acid to converge with that of ManNAc and GlcNAc at the common intermediate GlcNAc-6-P (p.53 1<sup>st</sup> column 2<sup>nd</sup> paragraph).

Further motivation is in Tabata et al. who teach pathways for the formation of NeuAc the development of a microbial transformation for the synthesis of NeuAc using bacterial cells, because N-acetyl-D-mannosamine (ManNAc) is very expensive and not readily available for large-scale (Abstract and Introduction 2<sup>nd</sup> column).

Even further motivation is in Ishige et al. who teach because CMP-NeuAc synthetase responsible for biosynthesis of CMP-NeuAc requires expensive CTP as a cytidyl donor, an enzymatic method to produce CMP-NeuAc should contain an appropriate CTP-generating system, and using yeast cells as CTP-generating system form CMP and CMP-NeuAc synthetase(p.1736 Introduction 2<sup>nd</sup> column).

Therefore, in view of the above teachings, it would have been obvious to one of ordinary skill in the art to modify the method of Koizumi et al. and use N-acetylglucosamine-6-phosphate 2-epimerase as taught by Plumbridge & Vimr in order to provide a process for producing CMP-N-acetylneuraminic acid (CMP-NeuAc). The motivation as taught by Koizumi et al. and Ishige et al. would be the potential of CMP-NeuAc, and NeuAc related compounds for the development of therapeutics, also to provide an efficient process useful for the production of CMP-NeuAc using inexpensive precursors.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on 9:00 am to 5:30 pm EST Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford Jr/  
Primary Examiner, Art Unit 1651

Kade Ariani  
Examiner  
Art Unit 1651